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Application No.: 09/980,697

REMARKS

This amendment responds to the office action of February 28, 2008 (the Office Action). Herein, claims 39, 41, 42 and 44-46 are amended and new claims 67 and 68 are added.

The Examiner has pointed out that the numbering of the previously submitted claim set was incorrect. Claims 44-66 have been renumbered to correct the omission of claim 43 in the last amendment. Old claim 43 is now new claim 68 with minor amendments for clarity. Please note that amending the phrase "a group or groups" to "a group" for clarity is not a narrowing amendment, with "a group" meaning one or more groups according to the customary usage of the article "a".

The claims have been amended to specify the biguanide-containing moiety as comprising a plurality of biguanide groups, as at, e.g., page 20 of the Application. The claims have also been amended to specify chemical binding of biguanide groups by one or more alternatives of a substituted urea linkage, a substituted thiourea linkage, a N,N-disubstituted amide linkage, a N,N-disubstituted aminal linkage, a N,N-disubstituted hemiaminal or aminal linkage, or a tertiary amine linkage, as at, e.g., original claims 4 or 9. New claim 67 finds support at, e.g., page 20 of the Application.

Claims 39-66 were rejected for lack of written description on the grounds related to the phrase "a tertiary amino group" (pages 2-3 in the Office Action). This phrase has been removed for clarity and to advance prosecution. Withdrawal of this rejection is requested.

Claims 39-66 were rejected for lack of written description on the grounds related to "-NH-C(NH)-NH-C(NH)-NH-" (pages 3-4 in the Office Action). This formula has been removed to advance prosecution since it is defined in the specification as a biguanide group and the claims are directed to biguanide groups in any event. The specification explains on page 4, lines 23-24 that biguanides are strongly basic compounds containing the biguanide group -NH-C(NH)-NH-C(NH)-NH-. The same passage goes on to explain that biguanides have powerful antimicrobial properties and that two embodiments of the Application are directed to polyhexanide and/or chlorhexidine. The structures of these two compounds are disclosed on page 5 and it can be seen that both formulae incorporate the biguanide group -NH-C(NH)-NH-C(NH)-NH-. The formula for a biguanide group is familiar to those of skill in the art such a skilled person would fully understand the meaning and scope of the amended claims. Withdrawal of this rejection is requested.

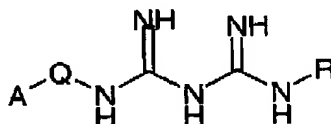
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The pending claims have been rejected under 35 U.S.C. §103(a) in light of U.S. Pat. No. 5,142,010 to Olstein ("Olstein") in combination with U.S. Pat. No. 5,451,424 to Solomon et al. ("Solomon et al.").

In general, an artisan following these references would not be able to make what is claimed because the references require highly distinct chemical structures not taught in the references, and also as further explained below. It is well-settled law that a prima facie case of rejection must point to prior art that enables the artisan to make what is claimed, but that is not the case for the present claims. Assertions in a prior art reference do not support an anticipation or obviousness rejection unless the references place the claimed invention in the hands of the public. Beckman Instruments Inc. v. LKB Produkter AB, 13 USPQ2d 1301, 1304 (Fed. Cir. 1989). "In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." Id. While a properly citable reference is prior art for all that it teaches, references along with the knowledge of a person of ordinary skill in the art must be enabling to place the invention in the hands of the public. In re Paulsen, 31 USPQ2d 1671, 1675 (Fed. Cir. 1994). See also In re Donohue, 226 USPQ 619, 621 (Fed. Cir. 1985).

Further, there would be no rationale for an artisan following the references to make what is claimed. As explained below, the claimed invention departs from merely substituting or combining prior art elements, or using known methods, to obtain a predictable result.

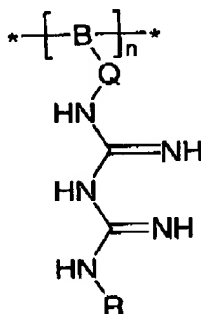
Olstein relates to polymeric biocidal agents formed from a biguanide-containing monomer. The monomer described by Olstein includes a biguanide group which is linked via a nitrogen atom at one terminus and has the following formula:



where A is a polymerizable group and Q is a linker e.g. phenylene (see column 2, lines 47-59). The polymerizable group A can be, for example an alkoxy silane moiety, an isocyanate moiety, a polymerizable vinyl moiety, an epoxy group, an aziridine group etc (see passage bridging columns 2 and 3 of Olstein). Several examples of monomers of this general formula are given by Olstein in columns 7-9

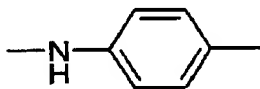
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It follows from the explanation of Olstein's monomer that the polymerised product will therefore be a chain with single pendant biguanide groups. A homopolymer would take the form:

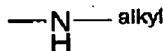


where B is the polymerised residue of the polymerizable group A and according to Olstein, copolymers are also possible.

Thus, the polymer of Olstein is a chain with single pendant biguanide groups. The group Q is generally a phenylene group, although it can also be an alkyl moiety or another aryl moiety (column 5, lines 34-44, where A-Q is defined as Z) and thus, as the Examiner has pointed out, it follows that the biguanide groups of Olstein must always be linked to the polymer chain via a secondary amine linkage, for example:



when Q is phenylene or

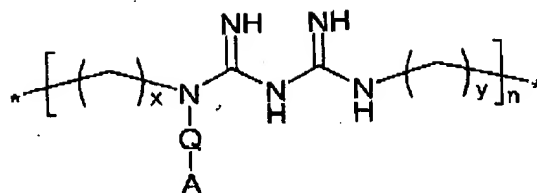


when Q is alkyl.

To summarize, the polymer of Olstein is a chain of monomer units with a single pendant biguanide group linked to each monomer unit via a secondary amine linkage.

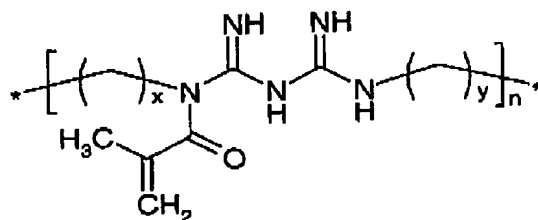
In contrast, what is claimed has a highly distinct structure that can be visualized as:

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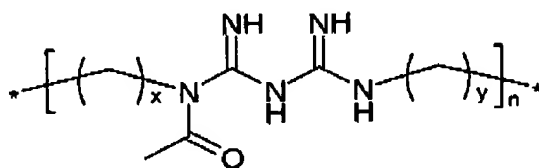
where, as with the Olstein patent, A is a polymerizable group and Q is a linker, e.g., thiourea, N-disubstituted amide or N,N-disubstituted amination linker; and x and y are integers (both are 3 for polyhexanide).

This type of structure is exemplified in Example 6, where the biguanide containing compound polyhexanide was reacted with methacryloyl chloride to form a monomer of the formula:



where the polyhexanide is linked to the methacrylate monomer via a tertiary amide (i.e. an N,N-disubstituted amide) linkage (see page 20 of the present specification).

This monomer is used in Examples 7 to 11 to form contact lenses and coatings of a polymethacrylate polymer, where each methacrylate unit has a pendant group:



Therefore, the claimed polymers differ from the polymers described by Olstein. One reason is that each monomer unit of the polymer incorporates a biguanide-containing moiety which comprises a plurality of, or multiple, biguanide groups rather than the single biguanide group of Olstein.

Similarly, please see also Example 12, which is similar to Example 6 except that each of the methacrylate monomer units is linked to a chlorhexidine residue rather than to a

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polyhexanide residue. Again, reaction of methacryloyl chloride with the secondary amine nitrogen of the chlorhexidine results in the formation of an N,N-disubstituted amide (also called a tertiary amide) bond.

Thus, for instance, present claim 39 differs from that of Olstein because, among other things, the polymer of Olstein has a single pendant biguanide group attached to each monomer unit *via* a secondary amine bond whereas the polymer of amended claim 1 of the present invention has a biguanide-containing moiety, i.e., a chain containing a plurality of, or multiple, biguanide groups, attached to each monomer unit *via* substituted urea linkage, or a substituted thiourea linkage, a N,N-disubstituted amide linkage, a N,N-disubstituted hemiaminal or aminal linkage, or a tertiary amine linkage.

In view of this, Applicant submits that the medical device of claim 41 formed from the polymer of the present invention must also be patentable over Olstein.

In paragraph 4 on page 5 of the Office Action, the Examiner has argued that in the polymer of Olstein "the reaction sites binding to the polymer include isocyanate" but Applicant submits that this is not the case. In the Olstein patent, the groups such as isocyanate to which the Examiner refers are in fact the polymerizable groups and not groups which can be used to link a biguanide to a polymer.

It is not possible using the chemistry described by Olstein to prepare polymers in which the pendant biguanide groups are attached via isocyanate or similar moieties on the polymer. This is because the chemistry used to form the polymers of Olstein is entirely different from that used by the present inventors. In the method of Olstein, the secondary amine linkage is present in the starting material used to form the biguanide-containing monomer (see columns 5-9 of Olstein) and is not formed during the linkage of the biguanide group to the polymerizable group.

The processes of the present invention are entirely different from that of Olstein. In the process of amended claim 45, reactive sites on a polymeric material are reacted with secondary amine groups of a biguanide group to form a substituted urea linkage, a substituted thiourea linkage, a N,N-disubstituted amide linkage or a N,N-disubstituted aminal linkage. This process is illustrated in Examples 3 and 4 of the present invention.

Alternatively, in the process of amended claim 49, a polymer precursor is modified by reacting some of the secondary amine nitrogen atoms of a biguanide group with reactive sites on a polymer precursor to form a substituted urea linkage, or a substituted thiourea linkage,

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or a N,N-disubstituted amide linkage or a N,N-disubstituted hemiaminal or aiminal linkage or a tertiary amine linkage. This process is illustrated in Examples 6 and 12.

The polymer of the present invention has an advantage over the product of Olstein in that it is possible to introduce the biguanide containing moiety either before or after the formation of the polymer backbone. This cannot be achieved using the polymer and method of Olstein.

A further advantage of the present invention over the polymer of Olstein, which is perhaps still more important, is that each monomer unit of a polymer of the present invention incorporates multiple biguanide groups rather than a single biguanide group as in the polymer of Olstein. Thus the present invention represents a way of increasing the number of biguanide groups which can be attached to a polymer chain.

In summary, Applicant submits that the polymer is both new and advantageous when compared to the polymer of Olstein. The polymer of the present invention could not be prepared by the process described by Olstein and has the advantage that it incorporates a larger number of biguanide groups for each monomer unit.

The process for preparing the polymer is also new and allows the biguanide-containing moiety to be introduced either before or after the polymerisation reaction.

The Examiner states in paragraph 5 on page 5 of the Office Action that the '424 patent (Solomon *et al*) discloses a biguanide polymer comprising chlorhexidine. With respect, Applicant does not agree that this is the case. In fact, Solomon *et al* discloses a melt formed from a substantially hydrophilic polymer and chlorhexidine. The components are thoroughly mixed in the melted state and then used to form anti-infective medical articles. The polymer may be a siloxane-urethane copolymer, a polyurethane or a polyurethaneurea (column 3, lines 1-3). When the melt is formed, there is no chemical reaction between the polymer and the chlorhexidine and the result is a physical mixture not a polymer containing chlorhexidine residues. The '424 (Solomon) discloses a mixture of a polymer and chlorhexidine and the '010 (Olstein) patent discloses a polymer incorporating a single biguanide unit per monomer. The two ideas are entirely different and a person of skill in the art would have no reason or basis for using Solomon *et al.* to make what is claimed.

In addition, the method used by Olstein for preparing his polymers could not have been used to incorporate chlorhexidine into his polymers. This is because Olstein forms the biguanide unit in his monomer from a monoguanido compound (column 5 of Olstein) which already incorporates the polymerizable part of the monomer linked to the guanide via a

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secondary amine linkage. The monoguanido compound is then reacted with a mono- or di-amine to form the biguanide (columns 5-6 of Olstein). The biguanide, which already contains the polymerizable group, is then polymerized (Olstein, column 7-8). This method could not therefore be used to incorporate chlorhexidine into a polymer and certainly could not be used to form, e.g., a substituted urea linkage, a substituted thiourea linkage, a N,N-disubstituted amide linkage or a N,N-disubstituted aminal linkage.

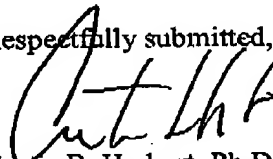
Thus, even if a person of skill in the art tried to combine the teachings of Olstein and Solomon, it would not have been possible to do so because the chemistry described by Olstein is not suitable for incorporating chlorhexidine into a polymer. Furthermore, Solomon does not even describe a polymer in which chlorhexidine is chemically incorporated. Please note that new claim 67 is directed specifically to chlorhexidine.

Applicant has now amended the claims so as to remove terms objectionable to the Examiner and to place the case in condition for allowance. The Examiner is respectfully requested to consider the amended claims and arguments submitted herewith.

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,



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